

Lectures on DNA Codes ⁰

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Abstract

For q -ary n -sequences, we develop the concept of similarity functions that can be used (for $q = 4$) to model a thermodynamic similarity on DNA sequences. A similarity function is identified by the length of a longest common subsequence between two q -ary n -sequences. Codes based on similarity functions are called DNA codes [1, 2, 3]. DNA codes are important components in biomolecular computing [4] and other biotechnical applications that employ DNA hybridization assays. The main aim of the given lecture notes – to discuss lower bounds on the rate of optimal DNA codes for a biologically motivated [2] similarity function called a block similarity and for the conventional deletion similarity function [5, 6, 7] used in the theory of error-correcting codes. We also present constructions of suboptimal DNA codes based on the parity-check code detecting one error in the Hamming metric [8].

1 Introduction and Biological Motivation

Single strands of DNA are, abstractly, (A, C, G, T) -quaternary sequences, with the four letters denoting the respective nucleic acids: *adenine* (A), *cytosine* (C), *guanine* (G), and *thymine* (T). Strands of DNA sequence are oriented; for instance, $X = AACG$ is distinct from $Y = GCAA$. Furthermore, DNA is ordinarily double stranded: each sequence X , or strand, occurs with its *reverse complement* X' , with reversal denoting that the sequences of the two strands are oppositely oriented, relative to one other, and with complementarity denoting that the allowed pairings of letters, opposing one another on the two strands, are (A, T) or (C, G) —the canonical Watson-Crick pairings. For instance, two sequences $X = AACG$ and $X' = CGTT$ are reverse complement of one another. Obviously, for any strand X , we have $(X')' = X$.

Whenever two, not necessarily complementary, oppositely directed DNA strands "mirror" one another, they are capable of coalescing into a DNA duplex which is based on hydrogen bonds between some pairs of nucleic acids. Namely, pair (A, T) forms *two* bonds, pair (C, G) forms *three* bonds, and any other pair is called a *mismatch* because it does not form any bond. The process of forming DNA duplexes from single strands is referred to as DNA *hybridization*. The greatest energy of DNA hybridization (the greatest stability of DNA duplex) is obtained when the two sequences are reverse complement of one another and the DNA duplex formed is a Watson-Crick (WC) duplex. However, there are many instances when the formation of non-WC duplexes are energetically favorable. The energy of DNA hybridization (the stability of DNA duplex) $\mathcal{E}(X, Y)$ of two single DNA strands X and Y is, to a first approximation, measured by the longest length of a common subsequence (not necessary contiguous) of either strand and the reverse complement of the other [1]. For two mutually reverse complementary strands X

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and X' of length n , this measure plainly equals their length n , i.e., the maximum number of Watson-Crick bonds (complementary letter pairs) which may be formed between two oppositely oriented strands:

$$\mathcal{E}(X, X') = \max_Y \mathcal{E}(X, Y') = \max_Y \mathcal{E}(Y', X) = \mathcal{E}(X', X) = n. \quad (1.1)$$

For instance, if $X = AACG$ and $X' = CGTT$, then $\mathcal{E}(X, X') = 4$.

A DNA code \mathbf{X} is a collection of N single stranded DNA sequences (codewords) of fixed length n where each strand occurs with its reverse complement and no strand in the code equals its reverse complement [1, 3], i.e., if $X \in \mathbf{X}$, then $X' \in \mathbf{X}$ and $X' \neq X$. In DNA hybridization assays, the general rule is that formation of WC duplexes is good, but the formation of non-WC duplexes is bad. A primary goal of DNA code design is to be assured that a fixed temperature can be found that is well above the melting point of all non-WC duplexes and well below the melting point of all WC duplexes that can form from strands in the code. Thus the formation of any WC duplex must be significantly more energetically favorable than all possible non-WC duplexes. Note [1] that for biotechnical applications, the code length n , $10 \leq n \leq 40$, is experimentally accessible and that codes with up to $N = 10^9$ codewords could soon be called for.

The following practical issue was an origin for the concept of DNA code. Assume that we have p types of some *molecular objects* and p *pools*. Each pool contains many identical copies (clones) of the corresponding object. We need to perform an experiment over all these pools. Since each experiment is expensive we are interested in the *junction* of these pools into one big *metapool* and performing only one experiment over this metapool. Then we face a problem of singling out some copies of each object from this mixture for analyzing experiment results.

For this purpose, there exists a method in which codewords of a DNA code \mathbf{X} of size N , where $N = 2p$ is an even number, are used as *tags*. We fix any p codewords $X(1), \dots, X(p)$ of \mathbf{X} which are called *capture tags* and the corresponding reverse complementary codewords $X'(1), \dots, X'(p)$ called *address tags*. Modern technologies allow to generate many copies of each tag and mark each molecular object by the corresponding tag. Then a metapool is created and an experiment is performed. We assume that these processes do not change capture tags.

After this a solid support is taken. It is divided into p separated zones. Many copies of an address tag $X'(i)$ are immobilized onto the corresponding i -th zone that physically segregates them. Then the support is placed into the metapool. This process is illustrated on Fig. 1.

Each pair of DNA sequences (codewords of DNA code \mathbf{X}) in a pool may form a duplex except immobilized address tags. In particular, any capture tag $X(i)$ may form a duplex with an address tag $X'(j)$. In this case, the corresponding object of the i -th type finds itself settled on the j -th zone of the support. Since there are many copies of each object and many copies of each address tag, one can finally find any type of object settled on j -th zone for any $j = 1, \dots, p$.

Let a stability function \mathcal{E} expresses the melting temperature of a duplex. Assume that for an index $j \in \{1, 2, \dots, p\}$ a certain temperature range separates large value $\mathcal{E}(X(j), X'(j))$ from small values $\mathcal{E}(X(i), X'(j))$ for $i \neq j$ and small values $\mathcal{E}(X(i), X(j)) = \mathcal{E}(X(i), (X'(j))')$ for any i and j . This means that there exists a temperature range at which all duplexes on the j -th zone melt except those which are formed by $X(j)$ and $X'(j)$. Finally, only the objects of the j -th type will be settled on the corresponding zone and that separates them from the other types, see Fig. 2. Whenever this condition holds for all values j , we are able to separate all types of objects.

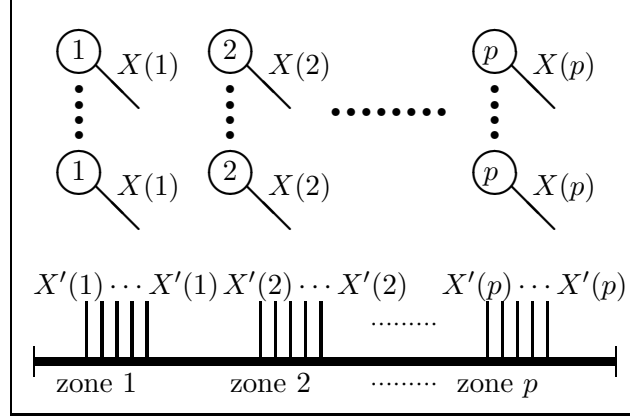


Figure 1: a metapool with capture tags $X(i)$ and address tags $X'(i)$

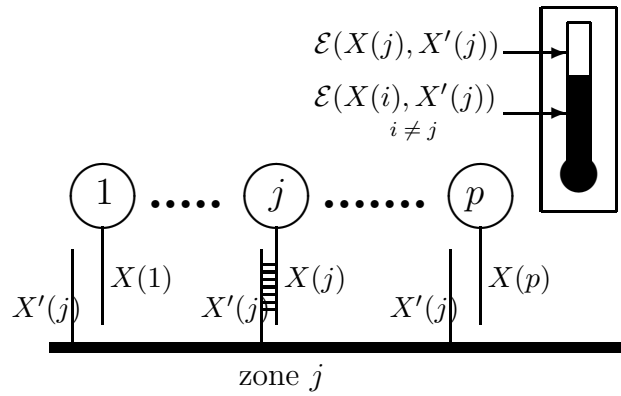


Figure 2: a separation of the j -th objects

The mathematical analysis of DNA hybridization is based on the concept of similarity functions that can be used to model a thermodynamic similarity on single stranded DNA sequences. For two quaternary n -sequences X and Y , the longest length of a sequence occurring as a (not necessary contiguous) subsequence of both is called a deletion similarity $S^\lambda(X, Y)$ between X and Y . We supposed [1, 3] that the deletion similarity $S^\lambda(X, Y)$ identifies the number of base pair bonds in a hybridization assay between X and the reverse complement of Y , i.e., the energy of DNA hybridization $\mathcal{E}(X, Y')$ satisfying (1.1) is defined as follows

$$\mathcal{E}(X, Y') = \mathcal{E}(X', Y) = S^\lambda(X, Y) = S^\lambda(Y, X). \quad (1.2)$$

Let D , $1 \leq D \leq n - 1$, be a fixed integer. A DNA code \mathbf{X} is called a DNA code of distance D based on deletion similarity or, briefly, an (n, D) -code [1, 3] if the deletion similarity

$$S^\lambda(X, Y) \leq n - D - 1 \quad \text{for any } X, Y \in \mathbf{X}, \quad Y \neq X. \quad (1.3)$$

Definition (1.2) and condition (1.3) mean that the energy of DNA hybridization

$$\mathcal{E}(X, Y') \leq n - D - 1 \quad \text{for any } X, Y \in \mathbf{X}, \quad Y \neq X,$$

i.e., any strand $X \in \mathbf{X}$ and the reverse complement of the other strand $Y \in \mathbf{X}$ can never form $\geq n - D$ base pair bonds in a hybridization assay. In the theory of deletion - correcting codes, condition (1.3), by itself, specifies codes capable to correct any combination of D deletions [5].

Example 1.1 DNA code $\mathbf{X} = \{X, X', Y, Y'\}$, where

$$X = ACAT, \quad X' = ATGT, \quad Y = ATAC, \quad Y' = GTAT, \quad (1.4)$$

is a (n, D) -code of length $n = 4$ and distance $D = 1$ because $n - D - 1 = 2$ and sequence $Z = AT$ of length 2 is the longest common subsequence between any pair of strands in DNA code \mathbf{X} . Hence,

$$\begin{aligned} \mathcal{E}(X, X) = \mathcal{E}(X', X') = S^\lambda(X, X') = 2, \quad \mathcal{E}(Y, Y) = \mathcal{E}(Y', Y') = S^\lambda(Y, Y') = 2, \\ \mathcal{E}(X, Y) = \mathcal{E}(X', Y') = S^\lambda(X, Y') = 2, \quad \mathcal{E}(X, Y') = \mathcal{E}(X', Y) = S^\lambda(X, Y) = 2. \end{aligned}$$

In paper [2], we introduced the concept of common block subsequence, namely: a common subsequence Z of sequences X and Y is called a common block subsequence if any two consecutive elements of Z which are consecutive in X are also consecutive in Y and vice versa. For two quaternary n -sequences X and Y , the longest length of a sequence occurring as a common block subsequence of both is called a block similarity between X and Y . For example, sequence $Z = AT$ of length 2 is the longest common block subsequence between any pair of strands in DNA code (1.4). Thus, DNA code (1.4) can be considered as DNA $(4, 1)$ -code based on block similarity.

The first conventional issue of coding theory [8] for DNA codes – to get a lower random coding bound on the rate of DNA codes and, hence, to identify values of the distance fraction D/n for which DNA code size grows exponentially when n increases. The given problem is more difficult than the corresponding problem for deletion - correcting codes. For instance, we cannot apply the best known random coding bounds [9] on the rate of deletion-correcting codes because these bounds were proved for codes which are not invariant under the reverse complement transformation. The second conventional issue of coding theory for DNA codes – to present constructions of DNA codes. The aim of our lecture notes is to discuss bounds and constructions for DNA codes based on the deletion and block similarities which have a good biological motivation to model a thermodynamic similarity on DNA sequences [2]. We will study q -ary DNA codes which are generalizations of quaternary DNA codes.

2 Notations, Definitions and Examples

The symbol \triangleq denotes definitional equalities and the symbol $[n] \triangleq \{1, 2, \dots, n\}$ denotes the set of integers from 1 to n . Let $q = 2, 4, \dots$ be a fixed even integer, $\mathbf{A} \triangleq \{0, 1, \dots, q-1\}$ be the standard alphabet of size $|\mathbf{A}| = q$ and $\lfloor u \rfloor$ ($\lceil u \rceil$) denote the largest (smallest) integer $\leq u$ ($\geq u$). Introduce the binary entropy function

$$h_q(u) \triangleq -u \log_q u - (1-u) \log_q(1-u), \quad 0 < u < 1.$$

Consider two arbitrary q -ary n -sequences

$$\mathbf{x} = (x_1, x_2, \dots, x_n) \in \mathbf{A}^n, \quad \mathbf{y} = (y_1, y_2, \dots, y_n) \in \mathbf{A}^n.$$

In what follows, we will denote by symbol $S = S(\mathbf{x}, \mathbf{y})$ an arbitrary symmetric function satisfying conditions

$$0 \leq S(\mathbf{x}, \mathbf{y}) = S(\mathbf{y}, \mathbf{x}) \leq S(\mathbf{x}, \mathbf{x}) = n, \quad \mathbf{x} \in \mathbf{A}^n, \quad \mathbf{y} \in \mathbf{A}^n, \quad (2.1)$$

and called [1] a *similarity* function. For instance, an *additive* similarity function

$$S^\alpha(\mathbf{x}, \mathbf{y}) \triangleq \sum_{i=1}^n S^\alpha(x_i, y_i), \quad \text{where} \quad S^\alpha(x, y) \triangleq \begin{cases} 1 & \text{if } x = y, \\ 0 & \text{if } x \neq y, \end{cases} \quad x, y \in \mathbf{A},$$

is the number of positions in which \mathbf{x} and \mathbf{y} coincide. Function $S^\alpha(\mathbf{x}, \mathbf{y})$ can be called the Hamming similarity because $n - S^\alpha(\mathbf{x}, \mathbf{y})$ is the well-known Hamming distance function (metric) applied in the theory of error-correcting codes [8].

Let $\ell \in [n]$ and $m = 1, 2, \dots, \ell$. By symbol

$$\mathbf{z} = (z_1, z_2, \dots, z_\ell) \in \mathbf{A}^\ell, \quad \text{where} \quad z_m = x_{i_m} = y_{j_m},$$

$$1 \leq i_1 < i_2 < \dots < i_\ell \leq n, \quad 1 \leq j_1 < j_2 < \dots < j_\ell \leq n,$$

we will denote a *common subsequence* of length $|\mathbf{z}| \triangleq \ell$ between \mathbf{x} and \mathbf{y} . By definition, the *empty* subsequence of length $|\mathbf{z}| \triangleq 0$ is a common subsequence between any sequences \mathbf{x} and \mathbf{y} .

Definition 1. [5]. Let $S^\lambda(\mathbf{x}, \mathbf{y})$, $0 \leq S^\lambda(\mathbf{x}, \mathbf{y}) \leq n$, denote the length $|\mathbf{z}|$ of *longest* common subsequence \mathbf{z} between sequences \mathbf{x} and \mathbf{y} . The number $S^\lambda(\mathbf{x}, \mathbf{y})$ is called a *deletion similarity* between \mathbf{x} and \mathbf{y} . Evidently, the function $S^\lambda = S^\lambda(\mathbf{x}, \mathbf{y})$ satisfies (2.1).

Definition 2. [2]. A common subsequence $\mathbf{z} = (z_1, z_2, \dots, z_\ell)$, $2 \leq \ell \leq n$, is called a *common block subsequence* of length $|\mathbf{z}| \triangleq \ell$ between \mathbf{x} and \mathbf{y} if any two consecutive elements z_m, z_{m+1} , $m = 1, 2, \dots, \ell-1$, which are consecutive (separated) in \mathbf{x} are also consecutive (separated) in \mathbf{y} and vice versa, i.e.,

$$(z_m = x_{i_m}, z_{m+1} = x_{i_{m+1}}) \leftrightarrow (z_m = y_{j_m}, z_{m+1} = y_{j_{m+1}}).$$

By definition, any common subsequence \mathbf{z} of length $|\mathbf{z}| = 0$ or $|\mathbf{z}| = 1$ is a common block subsequence. Let $S^\beta(\mathbf{x}, \mathbf{y})$, $0 \leq S^\beta(\mathbf{x}, \mathbf{y}) \leq n$, denote the length $|\mathbf{z}|$ of *longest* sequence occurring as a common block subsequence \mathbf{z} between sequences \mathbf{x} and \mathbf{y} . The number $S^\beta(\mathbf{x}, \mathbf{y})$ is called a *block similarity* between \mathbf{x} and \mathbf{y} . Obviously, $S^\beta = S^\beta(\mathbf{x}, \mathbf{y})$ satisfies (2.1) and

$$S^\beta(\mathbf{x}, \mathbf{y}) \leq S^\lambda(\mathbf{x}, \mathbf{y}), \quad \mathbf{x} \in \mathbf{A}^n, \quad \mathbf{y} \in \mathbf{A}^n.$$

Definition 3. [1, 3]. If $q = 2, 4, \dots$, then

$$\bar{x} \triangleq (q - 1) - x, \quad x \in \mathbf{A} = \{0, 1, \dots, q - 1\},$$

is called a *complement* of a letter x . For sequence $\mathbf{x} = (x_1, x_2, \dots, x_{n-1}, x_n) \in \mathbf{A}^n$, we define its *reverse complement* $\tilde{\mathbf{x}} \triangleq (\bar{x}_n, \bar{x}_{n-1}, \dots, \bar{x}_2, \bar{x}_1) \in \mathbf{A}^n$. Obviously, if $\mathbf{y} \triangleq \tilde{\mathbf{x}}$, then $\mathbf{x} = \tilde{\mathbf{y}}$ for any $\mathbf{x} \in \mathbf{A}^n$. If $\mathbf{x} = \tilde{\mathbf{x}}$, then \mathbf{x} is called a *self reverse complementary* sequence. If $\mathbf{x} \neq \tilde{\mathbf{x}}$, then a pair $(\mathbf{x}, \tilde{\mathbf{x}})$ is called a *pair of mutually reverse complementary* sequences.

Example 2.1. Let $q = 2$, $n = 8$ and

$$\mathbf{x} = (0, 1, 0, 1, 1, 0, 1, 1), \quad \mathbf{y} = (0, 0, 1, 0, 0, 1, 1, 0).$$

Obviously, $S^\alpha(\mathbf{x}, \mathbf{y}) = 2$. The deletion similarity $S^\lambda(\mathbf{x}, \mathbf{y}) = 6$ because 6-sequence

$$\mathbf{z} \triangleq (0, 1, 0, 1, 1, 0) = (x_1, x_2, x_3, x_4, x_5, x_6) = (y_2, y_3, y_4, y_6, y_7, y_8)$$

is the longest sequence occurring as a common subsequence between \mathbf{x} and \mathbf{y} . The block similarity $S^\beta(\mathbf{x}, \mathbf{y}) = 5$ because sequence

$$\mathbf{z} \triangleq (0, 1, 0, 1, 0) = (x_1, x_2, x_3, x_5, x_6) = (y_2, y_3, y_4, y_7, y_8)$$

is the longest sequence occurring as a common block subsequence between \mathbf{x} and \mathbf{y} .

Example 2.2. Let $q = 2$, $n = 10$ and

$$\mathbf{x} = (0, 1, 1, 0, 0, 0, 1, 1, 1, 1), \quad \mathbf{y} \triangleq \tilde{\mathbf{x}} = (0, 0, 0, 0, 1, 1, 1, 0, 0, 1)$$

be a pair of mutually reverse complementary sequences. We have $S^\alpha(\mathbf{x}, \mathbf{y}) = 4$. The deletion similarity $S^\lambda(\mathbf{x}, \mathbf{y}) = S^\lambda(\mathbf{x}, \tilde{\mathbf{x}}) = 8$ because the self reverse complementary sequence

$$\mathbf{z} \triangleq (0, 0, 0, 0, 1, 1, 1, 1) = \tilde{\mathbf{z}} = (x_1, x_4, x_5, x_6, x_7, x_8, x_9, x_{10}) = (y_1, y_2, y_3, y_4, y_5, y_6, y_7, y_{10})$$

is the longest sequence occurring as a common subsequence between \mathbf{x} and $\mathbf{y} \triangleq \tilde{\mathbf{x}}$. The block similarity $S^\beta(\mathbf{x}, \mathbf{y}) = S^\beta(\mathbf{x}, \tilde{\mathbf{x}}) = 6$ because the following self reverse complementary sequence

$$\mathbf{z} \triangleq (0, 0, 0, 1, 1, 1) = \tilde{\mathbf{z}} = (x_4, x_5, x_6, x_7, x_8, x_9) = (y_2, y_3, y_4, y_5, y_6, y_7)$$

is a longest sequence occurring as a common block subsequence between \mathbf{x} and $\mathbf{y} = \tilde{\mathbf{x}}$.

Let $\mathbf{x}(1), \mathbf{x}(2), \dots, \mathbf{x}(N)$, where $\mathbf{x}(k) \triangleq (x_1(k), x_2(k), \dots, x_n(k))$, $x_i(k) \in \mathbf{A}$, $k \in [N]$, be *codewords* of a q -ary *code* $\mathbf{X} = \{\mathbf{x}(1), \mathbf{x}(2), \dots, \mathbf{x}(N)\}$ of *length* n and *size* N , where $N = 2, 4, \dots$ be an *even* number. Let D , $1 \leq D \leq n - 1$, be an arbitrary integer.

Definition 4. [1, 2, 3]. A code \mathbf{X} is called a DNA (n, D) -code based on similarity function $S = S(\mathbf{x}, \mathbf{y})$ (briefly, (n, D) -code) if the following two conditions are fulfilled. (i) For any number $k \in [N]$ there exists $k' \in [N]$, $k' \neq k$, such that $\mathbf{x}(k') = \widetilde{\mathbf{x}(k)} \neq \mathbf{x}(k)$. In other words, \mathbf{X} is a collection of $N/2$ pairs of mutually reverse complementary sequences. (ii) For any $k, k' \in [N]$, where $k \neq k'$, the similarity $S(\mathbf{x}(k), \mathbf{x}(k')) \leq n - D - 1$. We will also say that code \mathbf{X} is a DNA code of length n , distance D and similarity $n - D - 1$.

For $q = 4$, a biological motivation of (n, D) -codes based on deletion similarity $S^\lambda = S^\lambda(\mathbf{x}, \mathbf{y})$ was suggested in [1]. If only condition (ii) is retained, then an (n, D) -code based on deletion

similarity is a code of length n capable to correct any combination of $\leq D$ deletions [5]. A biological motivation of quaternary DNA codes based on block similarity $S^\beta = S^\beta(\mathbf{x}, \mathbf{y})$ was suggested in [2].

For given n and D , we denote by $N_q(n, D)$ the *maximal size* of (n, D) -codes. If $d, 0 < d < 1$, is a fixed number, then

$$R_q(d) \triangleq \lim_{n \rightarrow \infty} \frac{\log_q N_q(n, \lfloor dn \rfloor)}{n} \quad (2.2)$$

is called a *rate* of $(n, \lfloor dn \rfloor)$ -codes.

We will use notations with upper indices $N_q^\lambda(n, D)$, $R_q^\lambda(d)$ and $N_q^\beta(n, D)$, $R_q^\beta(d)$ for the corresponding parameters of DNA codes based on similarity functions S^λ and S^β . From inequalities between considered similarity functions it follows that $N_q^\lambda(n, D) \leq N_q^\beta(n, D)$ and $R_q^\lambda(d) \leq R_q^\beta(d)$.

Remark 2.1. If $D = 1, 2 \dots$ is fixed and $n \rightarrow \infty$, then

$$N_q^\lambda(n, D) \leq \frac{D!}{(q-1)^D} \cdot \frac{q^n}{n^D} \cdot (1 + o(1)). \quad (2.3)$$

This upper bound follows from the corresponding results [5, 10, 11] (see, also [6], p. 272) obtained for codes capable to correct any combinations of $\leq D$ deletions.

Remark 2.2. One can easily understand that the conventional Hamming bound on the size of block codes with distance $D + 1$ is a trivial upper bound on $N_q^\beta(n, D)$, i.e.,

$$N_q^\beta(n, 1) \leq q^{n-1}, \quad N_q^\beta(n, D) \leq q^n \left/ \sum_{i=0}^{\lfloor D/2 \rfloor} \binom{n}{i} \cdot (q-1)^i \right., \quad D \geq 2.$$

For $D = 1$ an improvement of this trivial bound is given by

Theorem 2.1. *The maximal size $N_q^\beta(n, 1) \leq (q^{n-1} + q) / 2$.*

Proof of Theorem 2.1. Consider an arbitrary q -ary DNA code $\mathbf{X} = \{\mathbf{x}(k), k \in [N]\}$ of length n , distance $D = 1$ and block similarity $n - 2$. For each codeword $\mathbf{x}(k)$, there exists one or two tail subsequences of length $n - 1$ obtained by deletions of the first or the last element of $\mathbf{x}(k)$. Let \mathbf{X} contain N_1 ($N_2 = N - N_1$) codewords which yield one (two) tail subsequences of length $n - 1$. Obviously, $N_1 \leq q$. From item (ii) of Definition 4, it follows that there are $N_1 + 2N_2$ distinct tail subsequences of length $n - 1$. Thus one can write $N_1 + 2N_2 \leq q^{n-1}$, $N_1 \leq q$. These two inequalities lead to $N = N_1 + N_2 \leq \frac{q^{n-1} + q}{2}$.

Theorem 2.1 is proved.

Example 2.3. If $q = 2$ and $n = 4$, then a DNA code of length $n = 4$, size $N = 4$, distance $D = 1$ and block (deletion) similarity $n - D - 1 = 2$ contains 2 pairs of mutually reverse complementary codewords: **0000 1111** and **0110 1001**. Obviously, from Theorem 2.1 it follows that the given code has the maximal size and $N_2^\beta(4, 1) = N_2^\lambda(4, 1) = 4$.

3 Suboptimal DNA Codes for Distance $D = 1$

In this section, we assume that n is a number divisible by q , where $q = 2, 4, \dots$ is an *even* number. Hence, n is an *even* number as well. We also remind that the *complement* of a letter $a \in \mathbf{A} \triangleq \{0, 1, \dots, q-1\}$ is defined as $\bar{a} \triangleq (q-1) - a \in \mathbf{A}$. Therefore, $\bar{a} \neq a$ for any $a \in \mathbf{A}$. We say that a codeword $\mathbf{x} \in \mathbf{A}^n$ satisfies the parity-check condition if the arithmetic sum of its elements is a number divisible by q . Let $M_q(n)$ denote the set of all these codewords:

$$M_q(n) \triangleq \{\mathbf{x} = (x_1, x_2, \dots, x_n) \in \mathbf{A}^n : x_1 + \dots + x_n \equiv 0 \pmod{q}\}, \quad |M_q(n)| = q^{n-1}. \quad (3.1)$$

Any subset $T \subseteq M_n(q)$ is called a *parity-check code*. The set $M_n(q)$ is the optimal code of size q^{n-1} detecting one error in the Hamming metric [8]. It is called the *maximal parity-check code*. We will construct suboptimal DNA codes for distance $D = 1$ which are *subcodes* of $M_q(n)$. Obviously, for each codeword $\mathbf{x} \in M_q(n)$, its reverse complement $\tilde{\mathbf{x}} \in M_q(n)$.

3.1 Formulations of Results

In Sect. 3.2, we prove

Theorem 3.1. *There exists a q -ary DNA code of length n , distance $D = 1$, block similarity $n - D - 1 = n - 2$ and size*

- $N = \frac{1}{2} (q^{n-1} + q)$ if $n = qk$, $k = 1, 3, 5, \dots$;
- $N = \frac{1}{2} q^{n-1}$ if $q = 2^m$, $n = 2^{m+k}$, $k \geq 1$;
- $N \geq \frac{1}{2} \left(q^{n-1} - \frac{q^{n/2+1}-1}{q-1} \right)$ if $n = qk$, $k = 2, 4, 6, \dots$

Remark 3.1. If $n = qk$, where $k = 1, 3, 5, \dots$ is an arbitrary odd number, then Theorem 2.1 means that the construction of Theorem 3.1 is optimal. If q is fixed and $n \rightarrow \infty$, then Theorem 2.1 means that the construction of Theorem 3.1 is asymptotically optimal.

Example 3.1. For $n = q = 4$, the construction of optimal DNA code from Theorem 3.1 is illustrated by the following table which contains $4^3 = 64$ codewords satisfying the parity-check condition, namely: for each codeword, the sum of its elements is a number divisible by 4.

<u>0000, 3333</u>			
0013, 0233	3001, 2330	<u>1300, 3302</u>	0130, 3023
0031, 2033	1003, 0332	<u>3100, 3320</u>	0310, 3203
<u>0103, 0323</u>	3010, 3230	<u>0301, 2303</u>	1030, 3032
0112, 1223	2011, 2231	<u>1201, 2312</u>	1120, 3122
0121, 2123	1012, 1232	<u>2101, 2321</u>	1210, 3212
<u>0211, 2213</u>	1021, 2132	<u>1102, 1322</u>	2110, 3221
<u>0022, 1133</u>	2002, 1331	<u>2200, 3311</u>	0220, 3113
<u>0202, 1313</u>	2020, 3131		
<u>1111, 2222</u>			

These codewords are written as $\frac{1}{2} \cdot 4^3 = 32$ pairs of mutually reverse complementary codewords. Any row of the table consists of 1, 2, or 4 pairs. In any row, the first (second) codewords are obtained as consecutive left (right) cyclic shifts of the first (second) codeword of any fixed pair of the row. If we eliminate from the table all 15 pairs from the second and fourth columns of the table, then one can easily check that the rest 17 mutually reverse complementary pairs will constitute a quaternary DNA code \mathbf{X} of length $n = 4$, size $N = 2 \cdot 17 = 34$, block distance $D = 1$ and block similarity $n - D - 1 = 2$. We mark by the symbol "underline" pairs of codewords (there are 10 such pairs) from code X which have pairwise deletion similarities ≤ 2 . They constitute a quaternary DNA code of length $n = 4$, size $N = 2 \cdot 10 = 20$, deletion distance $D = 1$ and deletion similarity $n - D - 1 = 2$. This means that the maximal size $N_4^\lambda(4, 1) \geq 20$.

In Sect. 3.3, we prove

Theorem 3.2. *Let $n = qk$, where $q = 2, 4, \dots$ is an even number and $k = 1, 3, \dots$ is an odd number. Let there exists a parity-check code T , correcting single deletions, i.e., $T \subset M_n(q)$ and the deletion similarity $\mathcal{S}^\lambda(\mathbf{x}, \mathbf{y}) \leq n - 2$ for any $\mathbf{x}, \mathbf{y} \in T$, $\mathbf{x} \neq \mathbf{y}$. Then there exists a DNA $(n, 1)$ -code $T' \subset M_n(q)$ of size $|T'| \geq |T|$.*

We will use the following construction [10] of a parity-check code T correcting single deletions. **a)** Consider a partition of the set \mathbf{A}^n into q subsets $M^1(\beta)$, $\beta = 0, 1, \dots, q-1$, where

$$M^1(\beta) \triangleq \{\mathbf{x} = (x_1, x_2, \dots, x_n) \in \mathbf{A}^n : x_1 + \dots + x_n \equiv \beta \pmod{q}\}$$

In particular, the maximal parity-check code $M_n(q) = M^1(0)$. **b)** For each $\mathbf{x} \in \mathbf{A}^n$, we introduce a binary sequence $(\alpha_2, \dots, \alpha_n)$, where

$$\alpha_i \triangleq \begin{cases} 1 & \text{if } x_i \geq x_{i-1}, \\ 0, & \text{if } x_i < x_{i-1}, \end{cases} \quad i = 2, 3, \dots, n.$$

Consider a partition of the set \mathbf{A}^n into n subsets $M^2(\gamma)$, $\gamma = 0, 1, \dots, n$, where

$$M^2(\gamma) \triangleq \left\{ \mathbf{x} = (x_1, x_2, \dots, x_n) \in \mathbf{A}^n : \sum_{i=2}^n (i-1) \alpha_i \equiv \gamma \pmod{n} \right\}.$$

c) The intersection of two partitions defined in items **a)** and **b)** yields a partition of the set \mathbf{A}^n into nq subsets having the form $T(\beta, \gamma) \triangleq M^1(\beta) \cap M^2(\gamma)$. One can prove [10] that every subset of this partition is a code correcting single deletions. Hence, the size of a maximal code correcting single deletions exceeds $q^n / (nq) = q^{n-1} / n$.

If we fix $\beta = 0$, then we obtain a partition of the set $M_n(q)$ into n subsets of the form $T(0, \gamma)$, $0 \leq \gamma \leq n-1$. Each of these subsets can be applied as a parity-check code T for Theorem 3.2. If we choose a code having the maximal size

$$|T| = \max_{0 \leq \gamma \leq n-1} |T(0, \gamma)| \geq \frac{|M_n(q)|}{n} = \frac{q^{n-1}}{n},$$

then we obtain the following lower bound on the maximal size of DNA $(n, 1)$ -code.

Corollary. *If $n = qk$, where $k = 1, 3, \dots$ is an odd number, then*

$$N_q^\lambda(n, 1) \geq \frac{q^{n-1}}{n}.$$

Example 3.2. One can easily check that the following collection containing 11 pairs of mutually reverse complementary codewords:

0000	3333	1111	2222	0022	1133	2200	3311
0330	3003	1221	2112	0011	2233	1100	3322
0120	3123	1301	2302	0231	2013		

is a quaternary DNA code of length $n = 4$, size $N = 22$, deletion distance $D = 1$ and deletion similarity $n - D - 1 = 2$. Note that only the first 4 pairs satisfy the parity check condition (3.1).

Example 3.3. One can also easily check that the collection of 24 codewords:

0000	3333	1111	2222	0022	1133	2200	3311
0321	2103	2012	1231	0011	2233	1100	3322
3013	0230	0033	3300	1122	2211	1302	3120

is a quaternary code of length $n = 4$, size $N = 24$, deletion distance $D = 1$ and deletion similarity $n - D - 1 = 2$. This code is a code capable to correct single deletions. The given code is not a DNA code because the last 6 codewords of this code are self reverse complementary sequences.

Remark 3.2. One can prove that codes from Examples 3.2 and 3.3 are optimal codes, i.e., their sizes $N = 22$ and $N = 24$ are maximal possible for the corresponding codes of length $n = q = 4$. Proofs of these statements are omitted here because they are awkward and we do not know any generalizations for codes of length $n > 4$.

3.2 Proof of Theorem 3.1

The following important property of the maximal parity-check code $M_q(n)$ takes place.

Lemma 3.1. *If $n = qk$, where $k = 1, 3, \dots$, then code $M_q(n)$ does not contain self reverse complementary codewords.*

Proof of Lemma 3.1. By contradiction. Let there exist a codeword

$$\mathbf{x} = (x_1, x_2, \dots, x_n) = \widetilde{\mathbf{x}} \in M_q(n).$$

Then $x_{n-i+1} = q - 1 - x_i$, $i = 1, 2, \dots, n/2$, and the sum

$$\sum_{i=1}^n x_i = \sum_{i=1}^{n/2} [x_i + (q - 1 - x_i)] = \frac{n}{2}(q - 1) = \frac{qk}{2}(q - 1)$$

is a number divisible by q . This contradicts to the condition $k = 1, 3, \dots$.

Lemma 3.1 is proved.

For any sequence $\mathbf{x} \in \mathbf{A}^n$, we define its first *left cyclic shift* T_1 , i.e.,

$$T_1(\mathbf{x}) \triangleq (x_2, x_3, \dots, x_n, x_1) \in \mathbf{A}^n \quad \text{if} \quad \mathbf{x} = (x_1, x_2, \dots, x_n) \in \mathbf{A}^n.$$

Introduce the $(k + 1)$ -th left cyclic shift T_{k+1} , $k = 1, 2, \dots$, i.e., $T_{k+1}(\mathbf{x}) \triangleq T_1(T_k(\mathbf{x}))$. By the similar way we define the k -th *right cyclic shift* T_k , where $k < 0$. Let symbol T_0 be the identity

operator. For indices $i, k \in [n]$, we define index $i+k \in [n]$ as the corresponding sum by modulo n . Obviously, the i -th element of $T_k(\mathbf{x})$ has the form $T_k(\mathbf{x})_i = x_{i+k}$.

The set $\mathcal{O}(\mathbf{x}) \triangleq \{T_k(\mathbf{x}) : k = 0, 1, \dots, n-1\}$ containing all cyclic shifts of $\mathbf{x} \in \mathbf{A}^n$ is called an *orbit generated by \mathbf{x}* . Let $\ell(\mathbf{x}) \triangleq |\mathcal{O}(\mathbf{x})|$ denote the orbit size. Note that n is a number divisible by $\ell \triangleq \ell(\mathbf{x})$. For any $\mathbf{y} \in \mathcal{O}(\mathbf{x})$, the orbit $\mathcal{O}(\mathbf{y}) = \mathcal{O}(\mathbf{x})$, the size $\ell(\mathbf{y}) = \ell(\mathbf{x}) = \ell$, the ℓ -th shift $T_\ell(\mathbf{y}) = \mathbf{y}$ and $\mathcal{O}(\mathbf{x}) = \{T_k(\mathbf{x}) : k = 0, 1, \dots, \ell-1\}$.

In addition, it is easy to see that

$$\widetilde{T_k(\mathbf{x})} = T_{-k}(\widetilde{\mathbf{x}}), \quad \mathbf{x} \in \mathbf{A}^n, \quad k = 1, 2, \dots \quad (3.2)$$

It means that the set $\{\widetilde{\mathbf{y}} : \mathbf{y} \in \mathcal{O}(\mathbf{x})\}$ is an orbit generated by $\widetilde{\mathbf{x}}$. Thus, we obtain a *reverse complement operator* for orbits. If an orbit $\mathcal{O}(\mathbf{x})$ does not contain self reverse complementary sequences, then $\mathcal{O}(\mathbf{x}) \cap \mathcal{O}(\widetilde{\mathbf{x}}) = \emptyset$ and for any $\mathbf{y} \in \mathcal{O}(\mathbf{x})$, its reverse complement $\widetilde{\mathbf{y}} \in \mathcal{O}(\widetilde{\mathbf{x}})$. The given orbits $\mathcal{O}(\mathbf{x})$ and $\mathcal{O}(\widetilde{\mathbf{x}})$ are called *mutually reverse complementary orbits*.

If an orbit $\mathcal{O}(\mathbf{x})$ contains a self reverse complementary sequence, then $\mathcal{O}(\mathbf{x}) = \mathcal{O}(\widetilde{\mathbf{x}})$ and $\mathcal{O}(\mathbf{x})$ is called a *self reverse complementary orbit*. The following statement gives the structure of all self reverse complementary orbits.

Lemma 3.2. *If an orbit $\mathcal{O}(\mathbf{x}) = \mathcal{O}(\widetilde{\mathbf{x}})$, then the orbit size $\ell = \ell(\mathbf{x})$ is an even number and $\mathcal{O}(\mathbf{x})$ contains exactly two self reverse complementary sequences which are the $\ell/2$ -th cyclic shifts of each other. In addition, if these two self reverse complementary sequences (without loss of generality) are \mathbf{x} and $T_{\ell/2}(\mathbf{x})$, then the rest $\ell-2$ sequences from orbit $\mathcal{O}(\mathbf{x})$ can be divided into $(\ell-2)/2$ pairs of mutually reverse complementary sequences of the form*

$$(T_{\ell/2-i}(\mathbf{x}), T_{\ell/2+i}(\mathbf{x})), \quad \text{where} \quad T_{\ell/2+i}(\mathbf{x}) = \widetilde{T_{\ell/2-i}(\mathbf{x})}, \quad i = 1, 2, \dots, (\ell-2)/2. \quad (3.3)$$

Proof of Lemma 3.2. As far as $\widetilde{\mathbf{x}} \in \mathcal{O}(\mathbf{x})$ then there exists an integer $k, k = 0, 1, \dots, n-1$, for which the k -th cyclic shift $T_k(\mathbf{x}) = \widetilde{\mathbf{x}}$. Hence, for any $i = 1, 2, \dots, n$, the i -th coordinate of $T_k(\mathbf{x}) = \widetilde{\mathbf{x}}$ is $x_{i+k} = \overline{x_{n+1-i}}$.

Let k be an odd number. Since n is an even number we put the integer $i \triangleq \frac{n+1-k}{2}$. This leads to equality $x_{(n+1+k)/2} = \overline{x_{(n+1+k)/2}}$ which contradicts to the condition $\bar{a} \neq a, a \in \mathbf{A}$. Therefore, k is an even number, i.e., $k = 2t$.

Consider sequence $\mathbf{y} \triangleq T_t(\mathbf{x}) \in \mathcal{O}(\mathbf{x})$. Taking into account the above properties of \mathbf{x} , one can easily check that the i -th coordinate of \mathbf{y} is

$$(\mathbf{y})_i \triangleq y_i = x_{i+t} = x_{(i-t)+2t} = \overline{x_{n+1-(i-t)}} = \overline{x_{n+1-i+t}} = \overline{y_{n+1-i}} = (\widetilde{\mathbf{y}})_i, \quad i = 1, 2, \dots, n.$$

We have $\mathbf{y} = \widetilde{\mathbf{y}}$ and the ℓ -th shift $T_\ell(\mathbf{y}) = \mathbf{y} = \widetilde{\mathbf{y}}$ because $\mathbf{y} \in \mathcal{O}(\mathbf{x})$. This means that the orbit size $\ell = \ell(\mathbf{x}) = \ell(\mathbf{y})$ is an even number, i.e., $\ell = 2m$.

Let \mathbf{z} be an arbitrary self reverse complementary sequence and $\mathbf{z} = \widetilde{\mathbf{z}} \in \mathcal{O}(\mathbf{x})$. From (3.2) it follows

$$\widetilde{T_m(\mathbf{z})} = T_{-m}(\widetilde{\mathbf{z}}) = T_{-m}(\mathbf{z}) = T_{m-\ell}(\mathbf{z}) = T_m(T_{-\ell}(\mathbf{z})) = T_m(\mathbf{z}), \quad m = \ell/2.$$

On the other hand, let s be an arbitrary integer such that $T_s(\mathbf{z})$ be a self reverse complementary sequence. For any $i \in [n]$, we obtain

$$z_{i+2s} = z_{i+s+s} = (T_s(\mathbf{z}))_{i+s} = \widetilde{(T_s(\mathbf{z}))_{i+s}} = (T_{-s}(\widetilde{\mathbf{z}}))_{i+s} = (T_{-s}(\mathbf{z}))_{i+s} = z_i,$$

i.e., $T_{2s}(z) = z$. It follows that $2s$ is a number divisible by $\ell = 2m$ and s is a number divisible by $m = \ell/2$. Therefore, the orbit $\mathcal{O}(\mathbf{x})$ contains exactly two self reverse complementary sequences $\mathbf{y} \triangleq T_t(\mathbf{x})$ and $T_{\ell/2}(\mathbf{y})$. The form (3.3) for mutually reverse complementary sequences follows from (3.2).

Lemma 3.2 is proved.

Lemma 3.3. *For any codewords $\mathbf{x}, \mathbf{y} \in M_q(n)$, $\mathbf{x} \neq \mathbf{y}$, the block similarity $\mathcal{S}^\beta(\mathbf{x}, \mathbf{y}) = n - 1$ if and only if either $T_1(\mathbf{x}) = \mathbf{y}$ or $T_{-1}(\mathbf{x}) = \mathbf{y}$.*

Proof of Lemma 3.3. Let $\mathcal{S}^\beta(\mathbf{x}, \mathbf{y}) = n - 1$. Then \mathbf{x} and \mathbf{y} have a common block of length $n - 1$. Each of these codewords has an extra symbol which is either the first or the last symbol of the corresponding codeword. From the parity-check condition it follows that this extra symbol is the same in \mathbf{x} and \mathbf{y} and, hence, the given symbol is the first (last) symbol in \mathbf{x} (\mathbf{y}) or vice versa. In other words, $T_1(\mathbf{x}) = \mathbf{y}$ or $T_{-1}(\mathbf{x}) = \mathbf{y}$. The converse statement is evident.

Lemma 3.3 is proved.

Lemma 3.4. *Let $\mathcal{O}(\mathbf{x}) = \mathcal{O}(\tilde{\mathbf{x}}) \in M_q(n)$ and $\ell = \ell(\mathbf{x}) = 4k$. Then there exists a subset $\mathbf{X} \subset \mathcal{O}(\mathbf{x})$ of size $|\mathbf{X}| = 2k$ which is a DNA code of block similarity $n - 2$.*

Proof of Lemma 3.4. From Lemma 3.2 it follows that without loss of generality, we can assume that $\mathbf{x} = \tilde{\mathbf{x}}$. Define code

$$\mathbf{X} \triangleq \{T_m(\mathbf{x}) : m = 1, 3, \dots, \ell - 1\}.$$

Obviously, the size $|\mathbf{X}| = \frac{1}{2} \cdot |\mathcal{O}(\mathbf{x})| = \ell/2 = 2k$ because for any $\mathbf{y} \in \mathcal{O}(\mathbf{x})$, the s -th shift $T_s(\mathbf{y}) = \mathbf{y}$ if and only if s is a number divisible by $\ell = 4k$. In virtue of Lemma 3.2 and equality $\ell/2 = 2k$, the set \mathbf{X} does not contain self reverse complementary codewords. From (3.3) it follows that for codeword $\mathbf{y} = T_{\ell/2-i}(\mathbf{x}) \in \mathbf{X}$, codeword $\tilde{\mathbf{y}} = T_{\ell/2+i}(\mathbf{x}) \in \mathbf{X}$, $i = 1, 3, \dots, (\ell - 2)/2$. Finally, Lemma 3.3 shows that the block similarity of code \mathbf{X} does not exceed $n - 2$.

Lemma 3.4 is proved.

We divide the set $M_q(n)$, $n = qk$, into four nonintersecting subsets G_i , $i = 1, 2, 3, 4$. Subset G_1 contains all orbits of size $\ell = 1$. Subset G_2 contains all self reverse complementary orbits of size $\ell = 2$. Subset G_3 contains all self reverse complementary orbits of size $\ell = 4k$, $k = 1, 2, \dots$. Subset G_4 contains all other orbits. In virtue of Lemma 3.1, G_4 consists of all pairs of mutually reverse complementary orbits. For some values $n = qk$, subset G_2 and (or) subset G_3 are empty.

Obviously, $G_1 = \{\mathbf{x} = (a, a, \dots, a), a \in \mathbf{A}\}$ and the size $|G_1| = q$. The set G_1 is invariant under the reverse complement transformation and does not contain self reverse complementary codewords. The block similarity between any two codeword from G_1 is equal to zero. Therefore, G_1 satisfies DNA code definition.

1) Let $n = qk$, $k = 1, 3, 5, \dots$. In virtue of Lemma 3.1, the set $M_q(n)$ does not contain self reverse complementary codewords $\mathbf{x} = \tilde{\mathbf{x}}$. Hence, G_4 contains $q^{n-1} - q$ codewords and G_4 consists of mutually reverse complementary orbits $\mathcal{O}(\mathbf{x})$ and $\mathcal{O}(\tilde{\mathbf{x}})$.

We construct a required code \mathbf{X} in the following way. 1a) The set G_1 is included in \mathbf{X} . 1b) For each pair of mutually reverse complementary orbits $\mathcal{O}(\mathbf{x})$ and $\mathcal{O}(\tilde{\mathbf{x}})$, code \mathbf{X} contains one-half of their codewords having the following form:

$$(T_k(\mathbf{x}), T_{-k}(\tilde{\mathbf{x}})) : k = 0, 2, 4, \dots, \ell - 1, \quad \ell = \ell(\mathbf{x}) = \ell(\tilde{\mathbf{x}}).$$

Taking into account (3.2) and Lemma 3.3, it is easy to see that the code \mathbf{X} is a DNA code of block similarity $n - 2$. The size of \mathbf{X} has the form

$$|\mathbf{X}| = q + \frac{q^{n-1} - q}{2} = \frac{q^{n-1} + q}{2}.$$

2) Let $q = 2^m$ and $n = 2^{m+m'}$, $m' \geq 1$. In this case, G_2 contains self reverse complementary orbits of size $\ell = 2$ and codewords $\mathbf{x} \in G_2$ have the form

$$G_2 = \{\mathbf{x} : \mathbf{x} = (a, \bar{a}, a, \bar{a}, \dots, a, \bar{a}), a \in \mathbf{A}\}, \quad |G_2| = q.$$

Set G_4 consists of mutually reverse complementary orbits $\mathcal{O}(\mathbf{x})$ and $\mathcal{O}(\tilde{\mathbf{x}})$.

We construct a required code \mathbf{X} in the following way. 2a) The set G_1 is included in \mathbf{X} . 2b) Elements of G_2 are not included in \mathbf{X} . 2c) Code \mathbf{X} contains one-half of codewords from the set G_3 according to Lemma 3.3. 2d) Code \mathbf{X} contains one-half of codewords from the set G_4 having the form described in item 1b). Obviously, \mathbf{X} is a DNA code of block similarity $n - 2$. The size of \mathbf{X} has the form

$$|\mathbf{X}| = |G_1| + \frac{|G_3| + |G_4|}{2} = |G_1| + \frac{|M_q(n)| - |G_1| - |G_2|}{2} = q + \frac{q^{n-1} - 2q}{2} = q^{n-1}/2.$$

3) Let $n = qm$, where $m, q = 2, 4, \dots$ be an arbitrary even numbers. In this case, n is a number divisible by 4, i.e. $n = 4k$. Let $M_q^1(n) \subset M_q(n)$ be subcode of code $M_q(n)$, where $M_q^1(n)$ contains all orbits $\mathcal{O}(\mathbf{x}) \subset M_q(n)$ of size $\ell(\mathbf{x}) = n$. For any $\mathcal{O}(\mathbf{x}) \in M_q(n) \setminus M_q^1(n)$, the size $\ell(\mathbf{x}) \leq n/2 = 2k$. Obviously, the total size of all orbits $\mathcal{O}(\mathbf{x})$ for which $\ell(\mathbf{x}) = d$ does not exceed q^d . This leads to the inequality

$$|M_q(n) \setminus M_q^1(n)| \leq \sum_{d=1}^{2k} q^d = \frac{q^{2k+1} - 1}{q - 1} \quad \text{or} \quad |M_q^1(n)| \geq q^{n-1} - \frac{q^{n/2+1} - 1}{q - 1}.$$

For any $\mathcal{O}(\mathbf{x}) \in M_q^1(n)$, the size $\ell(\mathbf{x}) = n = 4k$. Therefore, according to the construction described in item 1b) and Lemma 3.4, we obtain a DNA code \mathbf{X} of block similarity $n - 2$ and size

$$|\mathbf{X}| \geq \frac{1}{2} \left(q^{n-1} - \frac{q^{n/2+1} - 1}{q - 1} \right).$$

Theorem 3.1 is proved.

3.3 Proof of Theorem 3.2

Let a sequence $\mathbf{x} \in \mathbf{A}^n$. We will say that an integer-valued vector

$$n(\mathbf{x}) = n = (n_0, n_1, \dots, n_{q-1}), \quad 0 \leq n_x \leq n, \quad \mathbf{x} \in \mathbf{A} = \{0, 1, 2, \dots, q-1\},$$

is a *composition* of \mathbf{x} if n_x is equal to the number of entries of the symbol $x \in \mathbf{A}$ in \mathbf{x} . The reverse complement transformation of a sequence \mathbf{x} leads to the reverse transformation of

its composition: $n(\widetilde{\mathbf{x}}) = \bar{n} \triangleq (n_{q-1}, \dots, n_1, n_0)$. In what follows, we will consider codewords $\mathbf{x} \in M_q(n)$ having compositions n for which

$$\sum_{x=0}^{q-1} n_x = n, \quad \sum_{x=0}^{q-1} x \cdot n_x \equiv 0 \pmod{q}. \quad (3.4)$$

Lemma 3.5. *If $\mathbf{x}, \mathbf{y} \in M_q(n)$ and $n(\mathbf{x}) \neq n(\mathbf{y})$, then $S^\lambda(\mathbf{x}, \mathbf{y}) \leq n - 2$.*

Proof of Lemma 3.5. By contradiction. Consider two arbitrary codewords $\mathbf{x}, \mathbf{y} \in M_q(n)$ with deletion similarity $S^\lambda(\mathbf{x}, \mathbf{y}) = n - 1$. Obviously, these codewords can be obtained by two distinct insertions of the same symbol into their common subsequence of length $n - 1$. Therefore, \mathbf{x} and \mathbf{y} should have the same composition that contradicts to the condition of Lemma 3.5.

Lemma 3.5 is proved.

Lemma 3.6. *Let $n = qk$, where $k = 1, 3, \dots$ be an arbitrary odd number. If composition n satisfies (3.4), then $n \neq \bar{n}$. In particular, code $M_q(n)$ does not contain self reverse complementary codewords.*

Proof of Lemma 3.6. By contradiction. Let there exist a composition n for which $n = \bar{n}$. It means that $n_x = n_{q-1-x}$, $x \in \mathbf{A}$, and the sum $\sum_{x=0}^{q-1} n_x = 2 \cdot \sum_{x=0}^{q/2} n_x = n$. Hence,

$$\sum_{x=0}^{q-1} x \cdot n_x = \sum_{x=0}^{q/2} [x + (q - 1 - x)] \cdot n_x = (q - 1) \cdot \sum_{x=0}^{q/2} n_x = \frac{(q - 1)n}{2} = \frac{(q - 1)qk}{2}.$$

In virtue of (3.4), the right-hand side is a number divisible by q . This contradicts to $k = 1, 3, \dots$

Lemma 3.6 is proved.

Let a subset $T \subset M_q(n)$ be a code correcting single deletions, i.e., for any codewords $\mathbf{x}, \mathbf{y} \in T$, $\mathbf{x} \neq \mathbf{y}$, the deletion similarity $S^\lambda(\mathbf{x}, \mathbf{y}) \leq n - 2$. We will prove that there exists a DNA code $T' \subset M_q(n)$, $|T'| \geq |T|$, having the same property.

Let T be a fixed code correcting single deletions. We choose a set of compositions \mathcal{N} satisfying (3.4) in the following way. Consider all composition pairs (n, \bar{n}) satisfying (3.4). In virtue of Lemma 3.6, $n \neq \bar{n}$ and the set $M(n) \triangleq \{\mathbf{x} \in M_q(n) : n(\mathbf{x}) = n\}$ does not contain self reverse complementary codewords. For any pair (n, \bar{n}) the set \mathcal{N} contains exactly one element of the pair, namely: if $|T \cap M(n)| \geq |T \cap M(\bar{n})|$, then \mathcal{N} contains n , and \mathcal{N} contains \bar{n} , otherwise. Introduce the set

$$M(n, T) \triangleq T \cap M(n) \subset M_q(n), \quad \widetilde{M(n, T)} \triangleq \{\widetilde{\mathbf{x}} : \mathbf{x} \in M(n, T)\} \subset M_q(n).$$

Then the set

$$T' \triangleq \bigcup_{n \in \mathcal{N}} M(n, T) \cup \widetilde{M(n, T)}$$

is a DNA code of size $|T'| \geq |T|$. From Lemma 3.5 it follows that for any codewords $\mathbf{x}, \mathbf{y} \in T'$ having distinct compositions, the deletion similarity $S^\lambda(\mathbf{x}, \mathbf{y}) \leq n - 2$. From construction of T' it follows that for any codewords $\mathbf{x}, \mathbf{y} \in T'$ having the same composition, we have $\mathbf{x}, \mathbf{y} \in T$ or $\widetilde{\mathbf{x}}, \widetilde{\mathbf{y}} \in T$. And, therefore, in this case the deletion similarity is $S^\lambda(\widetilde{\mathbf{x}}, \widetilde{\mathbf{y}}) = S^\lambda(\mathbf{x}, \mathbf{y}) \leq n - 2$.

Theorem 3.2 is proved.

4 Bounds for DNA Codes

4.1 Formulations of results

Theorem 4.1 presents lower bounds on the size $N_q^\lambda(n, D)$ and rate $R_q^\lambda(d)$ of DNA codes based on deletion similarity. Let $d = d_q^\lambda$, $0 < d_q^\lambda < (q-1)/q$, be the unique root of equation

$$\frac{1+d}{2} = d \log_q(q-1) + h_q(d).$$

Theorem 4.1. (i). If $D = 1, 2, \dots$ is fixed and $n \rightarrow \infty$, then

$$N_q^\lambda(n, D) \geq \frac{1}{4} \cdot D!^2 \cdot \left(\frac{q}{(q-1)^2} \right)^D \cdot \frac{q^n}{n^{2D}} \cdot (1 + o(1)). \quad (4.1)$$

(ii). If $0 < d < d_q^\lambda$, then the rate $R_q^\lambda(d) > 0$ and the lower bound

$$R_q^\lambda(d) \geq \underline{R}_q^\lambda(d) \triangleq 1 + d - 2[d \log_q(q-1) + h_q(d)], \quad 0 < d < d_q^\lambda, \quad (4.2)$$

holds.

Example 4.1. For the binary case, $d_2^\lambda = 0.13340$ and for the most important quaternary case, $d_4^\lambda = 0.27029$. In addition, $d_6^\lambda = 0.34902$ and $d_8^\lambda = 0.40324$.

Theorem 4.2 gives lower bounds on the size $N_q^\beta(n, D)$ and rate $R_q^\beta(d)$ of DNA codes based on the similarity of blocks. Let $v = v(d)$, $0 < v(d) < d$, be the unique root of equation

$$\left(\frac{1-d}{v} - 1 \right) \left(\frac{d}{v} - 1 \right)^2 = 1, \quad 0 < v < d < \frac{1}{2}. \quad (4.3)$$

One can easily understand that $v(d)$ is calculated using the following recurrent method: $w_1 \triangleq 2$,

$$w_{m+1} = 1 + \frac{1}{\sqrt{\frac{1-d}{d} w_m - 1}}, \quad m = 1, 2, \dots, \quad v(d) = \lim_{m \rightarrow \infty} w_m.$$

Define the function

$$E_q(d) \triangleq (1-d) h_q \left(\frac{v(d)}{1-d} \right) + 2d h_q \left(\frac{v(d)}{d} \right), \quad 0 < d < \frac{1}{2}. \quad (4.4)$$

Let d_q^β , $0 < d_q^\beta \leq 1/2$, be the unique root of equation $1-d = E_q(d)$.

Theorem 4.2. (i). If $D = 1, 2, \dots$ is fixed and $n \rightarrow \infty$, then

$$N_q^\beta(n, D) \geq \frac{1}{4} \cdot \frac{D!}{q^D} \cdot \frac{q^n}{n^D} \cdot (1 + o(1)). \quad (4.5)$$

(ii). If $0 < d < d_q^\beta$, then the rate $R_q^\beta(d) > 0$ and the following lower bound

$$R_q^\beta(d) \geq \underline{R}_q^\beta(d) \triangleq (1-d) - E_q(d), \quad 0 < d < d_q^\beta. \quad (4.6)$$

holds.

Theorem 4.2 will be proved in Sect. 4.3 with the help of a random coding method described in Sect. 4.2. We briefly present the similar proof of Theorem 4.1 in Sect. 4.4.

Example 4.2. We calculated $d_2^\beta = 0.17888$, $d_4^\beta = 0.35752$, $d_6^\beta = 0.44523$ and $d_8^\beta = 1/2$. It means that the critical points for block similarity exceed the corresponding critical points (see, Example 4.1) for deletion similarity.

4.2 Random Coding Method for DNA Codes

In this section, we develop a general random coding method for DNA codes. Let $\mathcal{S} = \mathcal{S}(\mathbf{x}, \mathbf{y})$ be an arbitrary similarity function (2.1). For integers $0 \leq s \leq n$, we define two sets

$$\mathcal{P}(n, s) \triangleq \{(\mathbf{x}, \mathbf{y}) \in \mathbf{A}^n \times \mathbf{A}^n : S(\mathbf{x}, \mathbf{y}) = s\}, \quad \bar{\mathcal{P}}(n, s) \triangleq \{\mathbf{x} \in \mathbf{A}^n : S(\mathbf{x}, \tilde{\mathbf{x}}) = s\}. \quad (4.7)$$

Consider two random sequences

$$\mathbf{u} = (u_1, u_2, \dots, u_n), \quad \mathbf{v} = (v_1, v_2, \dots, v_n),$$

with independent identically distributed components having the uniform distribution on \mathbf{A} . Obviously, the corresponding probability distributions of random variables $\mathcal{S}(\mathbf{u}, \mathbf{v})$ and $\mathcal{S}(\mathbf{u}, \tilde{\mathbf{u}})$ have the form:

$$\Pr\{\mathcal{S}(\mathbf{u}, \mathbf{v}) = s\} = \frac{|\mathcal{P}(n, s)|}{q^{2n}}, \quad \Pr\{\mathcal{S}(\mathbf{u}, \tilde{\mathbf{u}}) = s\} = \frac{|\bar{\mathcal{P}}(n, s)|}{q^n}, \quad 0 \leq s \leq n. \quad (4.8)$$

A lower bound on $N_q(n, D)$ called a *random coding bound* is formulated as

Lemma 4.1. *For any D , $1 \leq D \leq n - 1$, the number*

$$N_q(n, D) \geq \left\lfloor \frac{1/2 - P_1(n, D)}{2 \cdot P_2(n, D)} \right\rfloor - 1, \quad (4.9)$$

where

$$P_1(n, D) \triangleq \Pr\{S(\mathbf{u}, \tilde{\mathbf{u}}) \geq n - D\} = q^{-n} \sum_{t=0}^D |\bar{\mathcal{P}}(n, n - t)|. \quad (4.10)$$

$$P_2(n, D) \triangleq \Pr\{S(\mathbf{u}, \mathbf{v}) \geq n - D\} = q^{-2n} \sum_{t=0}^D |\mathcal{P}(n, n - t)|, \quad (4.11)$$

Proof of Lemma 4.1. Let $\mathbf{X} = \{\mathbf{x}(1), \mathbf{x}(2), \dots, \mathbf{x}(2N)\}$ be an arbitrary DNA code of length n and size $2N$. Without loss of generality, we put the codeword $\mathbf{x}(N + k) \triangleq \tilde{\mathbf{x}}(k)$ for any $k \in [N]$. In virtue of this, code \mathbf{X} satisfies the condition (i) of Definition 4. Note that code \mathbf{X} will satisfy the condition (ii) of Definition 4 if for an arbitrary pair of codewords $(\mathbf{x}(k), \mathbf{x}(k'))$, $k \neq k'$, the number

$$S(\mathbf{x}(k), \mathbf{x}(k')) \leq n - D - 1.$$

We will say that a pair of codewords $(\mathbf{x}(k), \mathbf{x}(k + N))$, $k = 1, 2, \dots, N$, is an *D-bad pair in code \mathbf{X}* if there exists a codeword $\mathbf{x}(k')$ for which

$$\text{either } S(\mathbf{x}(k), \mathbf{x}(k')) \geq n - D, \ k' \neq k, \text{ or } S(\mathbf{x}(k + N), \mathbf{x}(k')) \geq n - D, \ k' \neq k + N.$$

Otherwise, we will say that $(\mathbf{x}(k), \mathbf{x}(k + N))$, $k = 1, 2, \dots, N$, is an *D-good pair in code \mathbf{X}* .

Consider the *ensemble* of q -ary codes $\mathbf{X} = \{\mathbf{x}(1), \mathbf{x}(2), \dots, \mathbf{x}(2N)\}$ of length n and size $2N$, where codewords $\mathbf{x}(1), \mathbf{x}(2), \dots, \mathbf{x}(N)$ are composed of $n \cdot N$ independent identically distributed letters having the uniform distribution on \mathbf{A} . One can easily understand that for an arbitrary pair of random codewords $(\mathbf{x}(k), \mathbf{x}(k'))$, $k \neq k'$, the distribution of random variable

$S(\mathbf{x}(k), \mathbf{x}(k'))$ has the form (4.8). Hence, using notations (4.10)-(4.11) and the additive bound on the union probability, we have

$$\Pr\{\text{pair } (\mathbf{x}(k), \mathbf{x}(k+N)) \text{ is } D\text{-bad in code } \mathbf{X}\} \leq (2N-2)P_2(n, D) + P_1(n, D). \quad (4.12)$$

Introduce the integer

$$\tilde{N} \triangleq \left\lfloor \frac{1/2 - P_1(n, D)}{2 \cdot P_2(n, D)} \right\rfloor + 1.$$

Inequality (4.12) means that for the ensemble of q -ary codes \mathbf{X} of length n and size $2\tilde{N}$,

$$\Pr\{\text{pair } (\mathbf{x}(k), \mathbf{x}(k+\tilde{N})) \text{ is } D\text{-bad in code } \mathbf{X}\} \leq \frac{1}{2}, \quad k = 1, 2, \dots, \tilde{N},$$

i.e., for the given ensemble, the *average* number of D -good pairs $\geq \lfloor \tilde{N}/2 \rfloor$. Therefore, there exists an (n, D) -code of size $\geq 2\lfloor \tilde{N}/2 \rfloor \geq \tilde{N} - 2$. This yields (4.10).

Lemma 4.1 is proved.

For fixed parameter u , $0 \leq u \leq 1$, define functions

$$\rho(u) \triangleq \overline{\lim}_{n \rightarrow \infty} \frac{\log_q |\mathcal{P}(n, \lceil (1-u)n \rceil)|}{n} \quad \text{and} \quad \bar{\rho}(u) \triangleq \overline{\lim}_{n \rightarrow \infty} \frac{\log_q |\bar{\mathcal{P}}(n, \lceil (1-u)n \rceil)|}{n}$$

satisfying obvious inequalities $0 \leq \rho(u) \leq 2$ and $0 \leq \bar{\rho}(u) \leq 1$. One can easily understand that Lemma 4.1 yields a *random coding bound* on the rate (2.2) of $(n, \lfloor dn \rfloor)$ -codes which is given by

Lemma 4.2. *Let d , $0 < d < 1$, be fixed. If $\min_{0 \leq u \leq d} \{1 - \bar{\rho}(u)\} > 0$, then the rate*

$$R_q(d) \geq \min_{0 \leq u \leq d} \{2 - \rho(u)\}.$$

If we apply Lemmas 4.1 and 4.2 to a similarity function $\mathcal{S}(\mathbf{x}, \mathbf{y})$, then we need to investigate the corresponding sets (4.7). For instance, consider the additive similarity $S^\alpha(\mathbf{x}, \mathbf{y})$ which is defined as the number of positions i , $i = 1, 2, \dots, n$, where $x_i = y_i$. Let the corresponding sets (4.7) be $\mathcal{P}^\alpha(n, s)$ and $\bar{\mathcal{P}}^\alpha(n, s)$. It is easy to see that the set $\bar{\mathcal{P}}^\alpha(n, s)$ is empty if s is odd. The sizes of sets $|\mathcal{P}^\alpha(n, s)|$ and $|\bar{\mathcal{P}}^\alpha(n, s)|$, $s = 2, 4, \dots$, are calculated as follows:

$$|\mathcal{P}^\alpha(n, s)| = \binom{n}{s} q^s q^{n-s} (q-1)^{n-s} = q^n \binom{n}{s} (q-1)^{n-s},$$

$$|\bar{\mathcal{P}}^\alpha(n, s)| = |\mathcal{P}^\alpha(\lfloor n/2 \rfloor, s/2)|.$$

Thus, for any u , $0 < u < 1$, the \cap -convex function

$$\rho^\alpha(u) \triangleq \overline{\lim}_{n \rightarrow \infty} \frac{\log_q \left[q^n \binom{n}{\lceil (1-u)n \rceil} (q-1)^{n-\lceil (1-u)n \rceil} \right]}{n} = 1 + h_q(u) + u \log_q(q-1)$$

and the \cap -convex function $\bar{\rho}^\alpha(u) = \rho^\alpha(u)/2$. Obviously,

$$\max_{0 \leq u \leq 1} \rho^\alpha(u) = \rho^\alpha\left(\frac{q-1}{q}\right) = 2.$$

Therefore, if $0 < d < \frac{q-1}{q}$, then

$$\min_{0 \leq u \leq d} \{1 - \bar{p}^\alpha(u)\} = \frac{1}{2} \min_{0 \leq u \leq d} \{2 - p^\alpha(u)\} = \frac{1}{2} [1 - h_q(d) - d \log_q(q-1)] > 0.$$

Hence, applying Lemma 4.2, we get the following lower bound on the rate $R_q^\alpha(d)$ of DNA codes based on the additive similarity

$$R_q^\alpha(d) \geq 1 - h_q(d) - d \log_q(q-1), \quad 0 < d < \frac{q-1}{q}.$$

This bound coincides with the well-known Gilbert-Varshamov bound on the rate of q -ary error-correcting codes for the Hamming metric [8].

In Sect. 4.3 and 4.4, we will investigate the sizes of sets (4.7) for similarity functions \mathcal{S}^λ and \mathcal{S}^β . Applying this analysis, we will prove Theorems 4.1 and 4.2 with the help of Lemmas 4.1 and 4.2.

4.3 Proof of Theorem 4.2

Let s , $1 \leq s \leq n$, be an arbitrary integer and

$$\mathcal{P}^\beta(n, s) \triangleq \{(\mathbf{x}, \mathbf{y}) \in \mathbf{A}^n \times \mathbf{A}^n : \mathcal{S}^\beta(\mathbf{x}, \mathbf{y}) = s\}, \quad \bar{\mathcal{P}}^\beta(n, s) \triangleq \{\mathbf{x} \in \mathbf{A}^n : \mathcal{S}^\beta(\mathbf{x}, \tilde{\mathbf{x}}) = s\}$$

denote sets (4.7) for similarity of blocks $\mathcal{S}^\beta(\mathbf{x}, \mathbf{y})$.

For a fixed sequence $\mathbf{z} = (z_1, z_2, \dots, z_s) \in \mathbf{A}^s$, we introduce the concept of its *j-block partition*

$$\mathbf{z} = \{\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_{j-1}, \mathbf{b}_j\}, \quad j = 1, 2, \dots, \min\{s, n-s+1\}, \quad (4.13)$$

i.e., a partition of \mathbf{z} into j nonempty blocks, where each block contains *consecutive* elements of \mathbf{z} . Let $\mathbf{x} = (x_1, x_2, \dots, x_n) \in \mathbf{A}^n$, be a fixed q -ary n -sequence. Definition 2 means that a block partition \mathbf{z} of the form (4.13) is a block subsequence of \mathbf{x} if \mathbf{z} is a subsequence of \mathbf{x} , i.e.,

$$\mathbf{z} = (x_{i_1}, x_{i_2}, \dots, x_{i_{s-1}}, x_{i_s}), \quad 1 \leq i_1 < i_2 < \dots < i_{s-1} < i_s \leq n,$$

and all blocks $\{\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_{j-1}, \mathbf{b}_j\}$ consisting of consecutive elements of the sequence \mathbf{x} are separated in \mathbf{x} . In addition, if a pair $(\mathbf{x}, \mathbf{y}) \in \mathcal{P}^\beta(n, s)$ (a sequence $\mathbf{x} \in \bar{\mathcal{P}}^\beta(n, s)$), then there exists a block partition \mathbf{z} which is a common block subsequence between \mathbf{x} and \mathbf{y} (\mathbf{x} and $\tilde{\mathbf{x}}$), i.e., each of sequences \mathbf{x} and \mathbf{y} (\mathbf{x} and $\tilde{\mathbf{x}}$) contains separated blocks $\{\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_{j-1}, \mathbf{b}_j\}$ consisting of their consecutive elements.

Lemma 4.3. *For any s , $1 \leq s \leq n$, the size*

$$|\mathcal{P}^\beta(n, s)| \leq q^s \cdot \sum_{j=1}^{\min\{s, n-s+1\}} \binom{s-1}{j-1} \cdot \left[q^{n-s} \cdot \binom{n-s+1}{j} \right]^2. \quad (4.14)$$

Proof of Lemma 4.3. Let $M \geq 1$ and $N \geq 1$ be arbitrary integers. For $M \geq N$, denote by $W_1(M; N)$ the number of all ways to distribute M indistinguishable marbles in N boxes provided that all N boxes are nonempty. Denote by $W_2(M; N)$ the number of all ways to

distribute M indistinguishable marbles in N boxes if empty boxes are accepted. It is well-known that

$$W_1(M; N) = \binom{M-1}{N-1}, \quad M \geq N, \quad \text{and} \quad W_2(M; N) = \binom{M+N-1}{N-1}.$$

Obviously, for any $\mathbf{z} \in \mathbf{A}^s$, the number of all its j -block partitions of the form (4.13) is

$$W_1(s; j) = \binom{s-1}{j-1}, \quad j = 1, 2, \dots, \min\{s, n-s+1\}. \quad (4.15)$$

If $M = (n-s) - (j-1)$ and $N = j+1$, then we have $N + M - 1 = n - s + 1$, $N - 1 = j$ and

$$W_2((n-s) - (j-1); j+1) = \binom{n-s+1}{j} \quad (4.16)$$

is an upper bound on the cardinality of the following set of q -ary n -sequences. These n -sequences are obtained by $M = (n-s) - (j-1)$ insertions of a fixed M -collection of q -ary letters (marbles) into $N = j+1$ "spaces" generated by a fixed q -ary s -sequence \mathbf{z} having a fixed j -block partition (4.13), namely: the space before \mathbf{b}_1 , the space after \mathbf{b}_j and $j-1$ inter-block spaces of (4.13) which are marked by a fixed $(j-1)$ -collection of separating q -ary letters (marbles). The given interpretation of formulas (4.15)-(4.16) leads to (4.14).

Lemma 4.3 is proved.

For any fixed sequence $\mathbf{z} \in \mathbf{A}^s$ and its j -block partition (4.13), we introduce a *reverse complement* j -block partition

$$\tilde{\mathbf{z}} \triangleq \{\tilde{\mathbf{b}}_j, \tilde{\mathbf{b}}_{j-1}, \dots, \tilde{\mathbf{b}}_2, \tilde{\mathbf{b}}_1\}, \quad j = 1, 2, \dots, \min\{s, n-s+1\}.$$

Lemma 4.4. *The set $\bar{\mathcal{P}}^\beta(n, s)$ is empty if $s \geq 1$ is odd. If $s \geq 2$ is even and an n -sequence $\mathbf{x} \in \bar{\mathcal{P}}^\beta(n, s)$, then there exist an integer j , $j = 1, 2, \dots, \min\{s, n-s+1\}$ and a self-reverse complementary s -sequence $\mathbf{z} = \tilde{\mathbf{z}}$, $|\mathbf{z}| = s$, of the form (4.13) which is a common block subsequence between \mathbf{x} and $\tilde{\mathbf{x}}$ and \mathbf{z} has a self reverse complementary block partition*

$$\mathbf{z} = \{\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_{j-1}, \mathbf{b}_j\} = \{\tilde{\mathbf{b}}_j, \tilde{\mathbf{b}}_{j-1}, \dots, \tilde{\mathbf{b}}_2, \tilde{\mathbf{b}}_1\} = \tilde{\mathbf{z}},$$

i.e., block $\mathbf{b}_1 = \tilde{\mathbf{b}}_j$, block $\mathbf{b}_2 = \tilde{\mathbf{b}}_{j-1}$, ..., block $\mathbf{b}_{j-1} = \tilde{\mathbf{b}}_2$, and block $\mathbf{b}_j = \tilde{\mathbf{b}}_1$.

Proof of Lemma 4.4. Consider an arbitrary $\mathbf{x} \in \bar{\mathcal{P}}^\beta(n, s)$ and its reverse complement $\tilde{\mathbf{x}}$. Let a sequence $\mathbf{z} \in \mathbf{A}^m$, $m \in [s]$, be a block subsequence (BSS) of \mathbf{x} . Then one can easily see that \mathbf{z} is a BSS of $\tilde{\mathbf{x}}$ if and only if its reverse complement $\tilde{\mathbf{z}}$ is a BSS of \mathbf{x} . This means that the following two statements are equivalent.

1. The set $\bar{\mathcal{P}}^\beta(n, s)$ is empty if s is odd. If s is even and a block partition \mathbf{z} , $|\mathbf{z}| = s$, is a common BSS between \mathbf{x} and $\tilde{\mathbf{x}}$, then there exists a sequence $\mathbf{z}' = \tilde{\mathbf{z}}'$ of length $|\mathbf{z}'| = |\mathbf{z}| = s$ having a self-reverse complementary block partition \mathbf{z}' which is a common BSS between \mathbf{x} and $\tilde{\mathbf{x}}$.
2. The set $\bar{\mathcal{P}}^\beta(n, s)$ is empty if s is odd. If s is even and block partitions \mathbf{z} , $\tilde{\mathbf{z}}$ of length $|\mathbf{z}| = |\tilde{\mathbf{z}}| = s$ are BSS of \mathbf{x} , then there exists a sequence $\mathbf{z}' = \tilde{\mathbf{z}}'$ of length $|\mathbf{z}'| = |\mathbf{z}| = s$ having a self-reverse complementary block partition \mathbf{z}' which is a BSS of \mathbf{x} .

Obviously, statement 1 is equivalent to the statement of Lemma 4.4. Hence, to complete the proof of Lemma 4.4, we need to check statement 2. For any $s \in [n]$, one can write

$$\mathbf{z} = (x_{i_1}, x_{i_2}, \dots, x_{i_{s-1}}, x_{i_s}), \quad 1 \leq i_1 < i_2 < \dots < i_{s-1} < i_s \leq n,$$

and

$$\tilde{\mathbf{z}} = (x_{k_1}, x_{k_2}, \dots, x_{k_{s-1}}, x_{k_s}), \quad 1 \leq k_1 < k_2 < \dots < k_{s-1} < k_s \leq n,$$

where

$$x_{k_1} = \bar{x}_{i_s}, \quad x_{k_2} = \bar{x}_{i_{s-1}}, \quad \dots, \quad x_{k_{s-1}} = \bar{x}_{i_2}, \quad x_{k_s} = \bar{x}_{i_1}. \quad (4.17)$$

Let $s \geq 1$ be an odd integer. From (4.17) it follows $x_{k_{\lceil s/2 \rceil}} = \bar{x}_{i_{\lceil s/2 \rceil}}$. Hence, $i_{\lceil s/2 \rceil} \neq k_{\lceil s/2 \rceil}$ because for any element $x \in \mathbf{A} = \{0, 1, \dots, q-1\}$, $q = 2, 4, \dots$, its complement $\bar{x} \triangleq (q-1)-x \neq x$. Without loss of generality, we say $i_{\lceil s/2 \rceil} < k_{\lceil s/2 \rceil}$. Then, in virtue of (4.17), the q -ary sequence

$$\mathbf{z}' \triangleq (x_{i_1}, x_{i_2}, \dots, x_{i_{\lceil s/2 \rceil}}, x_{k_{\lceil s/2 \rceil}}, \dots, x_{k_{s-1}}, x_{k_s})$$

of length $\lceil s/2 \rceil + \lceil s/2 \rceil = s+1$ is a self-reverse complementary common BSS between \mathbf{x} and $\tilde{\mathbf{x}}$. This contradicts to the condition $\mathbf{x} \in \bar{\mathcal{P}}^\beta(n, s)$, i.e., the set $\bar{\mathcal{P}}^\beta(n, s)$ is empty if s is odd.

Let $s = 2t$, $t = 1, 2, \dots$ be an even integer. Without loss of generality, we say

$$\frac{i_t + i_{t+1}}{2} \leq \frac{k_t + k_{t+1}}{2}, \quad \text{i.e., } i_t < k_{t+1} \quad \text{because } i_t < i_{t+1} \quad \text{and} \quad k_t < k_{t+1}.$$

Then, in virtue of (4.17), the q -ary sequence $\mathbf{z}' \triangleq (x_{i_1}, x_{i_2}, \dots, x_{i_t}, x_{k_{t+1}}, \dots, x_{k_{s-1}}, x_{k_s})$ of length $s = 2t$ is a self-reverse complementary BSS of \mathbf{x} .

Statement 2 and Lemma 4.4 are proved.

Lemma 4.4 and the arguments used for Lemma 4.3 lead to

Lemma 4.5. *For any even s , $s \in [n]$, the size*

$$|\bar{\mathcal{P}}^\beta(n, s)| \leq q^{s/2} \cdot \sum_{j=1}^{\min\{s, n-s+1\}} \binom{s/2-1}{\lceil j/2 \rceil - 1} \cdot \left[q^{n-s} \binom{n-s+1}{j} \right].$$

For $s \in [n]$, consider numbers

$$B(n, s) \triangleq \max_{1 \leq j \leq \min\{s, n-s+1\}} \left\{ \binom{s-1}{j-1} \cdot \binom{n-s+1}{j}^2 \right\}. \quad (4.18)$$

Proof of Statement (i) of Theorem 4.2. If $n \rightarrow \infty$, $k = 0, 1, 2, \dots$ is fixed and $s = n - k$, then the maximum in (4.18) is asymptotically achieved at $j = n - s + 1 = k + 1$ and the maximal value

$$B(n, n - k) = \frac{n^k}{k!} \cdot (1 + o(1)).$$

Hence, Lemma 4.3 yields the asymptotic inequality

$$|\mathcal{P}^\beta(n, n - k)| \leq q^{2n} \cdot \frac{n^k q^k}{k! q^n} \cdot (1 + o(1)), \quad n \rightarrow \infty, \quad k = 0, 1, 2, \dots$$

If $n \rightarrow \infty$ and $D = 1, 2, \dots$ is fixed, then definition (4.11) means that

$$P_2(n, D) \triangleq q^{-2n} \sum_{k=0}^D |\mathcal{P}^\beta(n, n-k)| \leq \frac{n^D q^D}{D! q^n} \cdot (1 + o(1)).$$

The similar arguments using Lemma 4.5 and definition (4.10) show that

$$P_1(n, D) \triangleq q^{-n} \sum_{k=0}^D |\bar{\mathcal{P}}^\beta(n, n-k)| = o(1).$$

Thus, Lemma 4.1 yields (4.5).

Statement (i) of Theorem 4.2 is proved.

Proof of Statement (ii) of Theorem 4.2. Let $u, 0 < u < 1$, be fixed parameter. Define the function

$$E_q(u) \triangleq \lim_{n \rightarrow \infty} \frac{\log_q B(n, \lceil (1-u)n \rceil)}{n}, \quad 0 < u < 1.$$

Lemmas 4.3 and 4.5 yield upper bounds on functions $\mathbf{p}^\beta(u)$ and $\bar{\mathbf{p}}^\beta(u)$ used in Lemma 4.2:

$$\begin{aligned} \mathbf{p}^\beta(u) &\triangleq \overline{\lim}_{n \rightarrow \infty} \frac{\log_q |\mathcal{P}^\beta(n, \lceil (1-u)n \rceil)|}{n} \leq (1+u) + E_q(u), \\ \bar{\mathbf{p}}^\beta(u) &\triangleq \overline{\lim}_{n \rightarrow \infty} \frac{\log_q |\bar{\mathcal{P}}^\beta(n, \lceil (1-u)n \rceil)|}{n} \leq \frac{1}{2} [(1+u) + E_q(u)]. \end{aligned}$$

Therefore, Lemma 4.2 gives a random coding bound on the rate $R_q^\beta(d)$ of q -ary DNA $(n, \lfloor dn \rfloor)$ -codes based on the block similarity. One can easily check that the given lower bound $\underline{R}_q^\beta(d)$ can be written in the form

$$R_q^\beta(d) \geq \underline{R}_q^\beta(d) = (1-d) - E_q(d), \quad E_q(d) = \max_{0 \leq v \leq d} F_q(v, d), \quad (4.19)$$

where

$$F_q(v, d) \triangleq (1-d) h_q\left(\frac{v}{1-d}\right) + 2d h_q\left(\frac{v}{d}\right).$$

The derivative of the binary entropy function $h_q(v)$ is

$$h'_q(v) = \log_q \frac{1-v}{v}, \quad 0 < v < 1.$$

Thus, the partial derivative of the function $F_q(v, d)$ is

$$\frac{\partial F_q(v, d)}{\partial v} = \log_q \frac{(1-d) - v}{v} + 2 \log_q \frac{d-v}{v} = \log_q \frac{[(1-d) - v](d-v)^2}{v^3}$$

and for a fixed $d, 0 < d < 1/2$, equation $\partial F_q(v, d)/\partial v = 0$ is equivalent to equation (4.3). The binary entropy function $h_q(v)$ is \cap -convex function of parameter $v, 0 < v < 1$. Hence, formulas (4.3)-(4.4) give the solution of the maximization problem (4.19) for \cap -convex function $F_q(v, d)$ of parameter $v, 0 \leq v \leq d$. This yields (4.6).

Theorem 4.2 is proved.

4.4 Proof of Theorem 4.1

Let $s, 0 \leq s \leq n$, be an arbitrary integer and

$$\mathcal{P}^\lambda(n, s) \triangleq \{(\mathbf{x}, \mathbf{y}) : S^\lambda(\mathbf{x}, \mathbf{y}) = s\}, \quad \bar{\mathcal{P}}^\lambda(n, s) \triangleq \{\mathbf{x} : S^\lambda(\mathbf{x}, \tilde{\mathbf{x}}) = s\}$$

denote the sets from Lemma 4.1 for the deletion similarity. An upper bound on the size $|\mathcal{P}^\lambda(n, s)|$ is based on the following well-known [6, 7] result.

Lemma 4.6. [6, 7]. *Let n and s be integers, $0 \leq s \leq n$. For an arbitrary sequence $\mathbf{y} \in \mathbf{A}^s$ denote by $\mathbf{B}_q(\mathbf{y}, n)$ the set of all sequences $\mathbf{x} \in \mathbf{A}^n$ that include \mathbf{y} as a subsequence, i.e., that can be obtained from \mathbf{y} by $n - s$ insertions. Then for the fixed n and s , the size of $\mathbf{B}_q(\mathbf{y}, n)$ does not depend on \mathbf{y} and has the form*

$$|\mathbf{B}_q(\mathbf{y}, n)| = \sum_{k=0}^{n-s} \binom{n}{k} (q-1)^k \triangleq B_q(n, s). \quad (4.20)$$

Proof of Lemma 4.6. We will use the induction over s . For $s = 0$ and $s = 1$, Lemma 4.4 is trivial. Assume that Lemma 4.4 is proved for all integers less than $s \geq 2$. Consider an arbitrary s -sequence $\mathbf{y} = (y_1, y_2, \dots, y_s)$ and its $(s-1)$ -subsequence $\mathbf{y}' \triangleq (y_2, y_3, \dots, y_s)$. Divide the set $\mathbf{B}_q(\mathbf{y}, n)$ into the sum of mutually disjoint sets $\mathbf{B}_q^k(\mathbf{y}, n)$, $k = 1, 2, \dots, n - s + 1$, where the set $\mathbf{B}_q^k(\mathbf{y}, n)$ is composed of n -sequences $\mathbf{x} = (x_1, x_2, \dots, x_n) \in \mathbf{B}_q(\mathbf{y}, n)$ such that $x_i \neq y_1$ for $i = 1, 2, \dots, k-1$ and $x_k = y_1$. Obviously, any such sequence \mathbf{x} belongs to the set $\mathbf{B}_q(\mathbf{y}, n)$ if and only if the $(n-k)$ -sequence $(x_{k+1}, x_{k+2}, \dots, x_n)$ contains \mathbf{y}' . In virtue of the induction hypothesis, the size

$$|\mathbf{B}_q^k(\mathbf{y}, n)| = (q-1)^{k-1} |\mathbf{B}_q(\mathbf{y}', n-k)| = (q-1)^{k-1} B_q(n-k, s-1),$$

i.e., for any $k = 1, 2, \dots, n - s + 1$, the size $|\mathbf{B}_q^k(\mathbf{y}, n)|$ is the same for all s -sequences \mathbf{y} . This means that the size $|\mathbf{B}_q(\mathbf{y}, n)|$ does not depend on \mathbf{y} as well. To complete the proof, we consider the s -sequence $\mathbf{y} = (0, 0, \dots, 0)$ for which the equality of Lemma 4.4 is trivial.

Lemma 4.6 is proved.

Lemma 4.7. *The set $\bar{\mathcal{P}}^\lambda(n, s)$ is empty if s is odd. If s is an even number and a sequence $\mathbf{x} \in \bar{\mathcal{P}}^\lambda(n, s)$, then there exists a self reverse complementary sequence $\mathbf{z} = \tilde{\mathbf{z}}$, $|\mathbf{z}| = s$, which is a common subsequence between \mathbf{x} and $\tilde{\mathbf{x}}$.*

The proof of Lemma 4.7 is omitted here because it can be easily obtained by an evident modification of our arguments used for Lemma 4.4.

Lemmas 4.6 and 4.7 yield

$$|\mathcal{P}^\lambda(n, s)| \leq q^s \cdot [B_q(n, s)]^2, \quad |\bar{\mathcal{P}}^\lambda(n, s)| \leq q^{s/2} \cdot B_q(n, s), \quad 0 \leq s \leq n. \quad (4.21)$$

Applying (4.20)-(4.21), Lemma 4.1 and arguments for Statement (i) of Theorem 4.2, one can easily prove (4.1), i.e., Statement (i) of Theorem 4.1.

If $u, 0 \leq u \leq (q-1)/q$, is fixed, then from definition (4.20) it follows

$$\lim_{n \rightarrow \infty} \frac{\log_q B_q(n, \lceil (1-u)n \rceil)}{n} = u \log_q(q-1) + h_q(u).$$

Therefore, applying (4.21), we have

$$p^\lambda(u) \triangleq \overline{\lim}_{n \rightarrow \infty} \frac{\log_q |\mathcal{P}^\lambda(n, \lceil (1-u)n \rceil)|}{n} \leq 1 - u + 2u \log_q(q-1) + 2h_q(u) \quad (4.22)$$

and

$$\bar{p}^\lambda(u) \triangleq \overline{\lim}_{n \rightarrow \infty} \frac{\log_q |\bar{\mathcal{P}}^\lambda(n, \lceil (1-u)n \rceil)|}{n} \leq \frac{1}{2} \cdot [1 - u + 2u \log_q(q-1) + 2h_q(u)], \quad (4.23)$$

provided that $0 < u \leq (q-1)/q$. Hence, if $0 < d < (q-1)/q$, then from (4.22)-(4.23) it follows

$$\min_{0 \leq u \leq d} \{1 - \bar{p}^\lambda(u)\} \geq \frac{1}{2} \cdot [1 + d - 2d \log_q(q-1) - 2h_q(d)], \quad (4.24)$$

$$\min_{0 \leq u \leq d} \{2 - p^\lambda(u)\} \geq 1 + d - 2d \log_q(q-1) - 2h_q(d). \quad (4.25)$$

Inequalities (4.24)-(4.25) and Lemma 4.2 yield (4.2), i.e., Statement (ii) of Theorem 4.1.

Theorem 4.1 is proved.

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